Claims

1 A method for the diagnosis of a polymorphism in $P2X_7$ in a human, which method comprises determining the sequence of the human at one or more of the following positions:

positions 936, 1012, 1147, 1343 and 1476 in the 5'UTR region of the $P2X_7$ gene as defined by the position in SEQ ID NO: 1;

positions 253, 488, 489, 760, 835, 853, 1068, 1096, 1315, 1324, 1405, 1448, 1494, 1513, 1628 and 1772 in the coding region of the $P2X_7$ gene as defined by the position in SEQ ID NO: 2; and

positions 4780, 4845, 4849, 5021, 5554, 5579, 5535, 5845 and 6911 in the intron region of the $P2X_7$ gene as defined by the position in SEQ ID NO: 3;

positions 76 ,155, 245, 270, 276, 348, 357, 430, 433, 460, 490 and 496 in the $P2X_7$ polypeptide as defined by the position in SEQ ID NO: 4;

and determining the status of the human by reference to polymorphism in $P2X_7$.

2 Use of a diagnostic method as defined in claim 1 to assess the pharmacogenetics of a drug acting at $P2X_7$.

3 A polynucleotide comprising at least 20 bases of the human $P2X_7$ gene and comprising an allelic variant selected from any one of the following:

Region	Variant SEQ ID NO: 1
5'UTR	936 A 1012 C 1147 G 1343 A 1476 G

Region	Variant SEQ ID NO: 2
exon 2	253 C
exon 5	488 A 489 T
exon 7	760 G
exon 8	835 A 853 A
exon 11	1068 A 1096 G
exon 12	1315 G
exon 13	1324 T 1405 G

	1448 T 1494 G 1513 C 1628 T 1772 A

Region	Variant SEQ ID NO: 3
intron E	4780 T 4845 T 4849 C
intron F	5021 C 5554 $(GTTT)_n$, n=4 5579 C 5535 T
intron G	5845 T 6911 C

4 A nucleotide primer which can detect a polymorphism as defined in claim 1.

5 An allele specific primer capable of detecting a $P2X_7$ gene polymorphism as defined in claim 1.

6 An allele-specific oligonucleotide probe capable of detecting a $P2X_7$ gene polymorphism as defined in claim 1.

7 Use of a $P2X_7$ gene polymorphism as defined in claim 1 as a genetic marker in a linkage study.

8 A method of treating a human in need of treatment with a drug acting at $P2X_7$ in which the method comprises:

i) diagnosis of a polymorphism in $P2X_7$ in the human, which diagnosis preferably comprises determining the sequence at one or more of the following positions:

positions 936, 1012, 1147, 1343 and 1476 in the 5'UTR region of the $P2X_7$ gene as defined by the position in SEQ ID NO: 1;

positions 253, 488, 489, 760, 835, 853, 1068, 1096, 1315, 1324, 1405, 1448, 1494, 1513, 1628 and 1772 in the coding region of the $P2X_7$ gene as defined by the position in SEQ ID NO: 2; and

positions 4780, 4845, 4849, 5021, 5554, 5579, 5535, 5845 and 6911 in the intron region of the $P2X_7$ gene as defined by the position in SEQ ID NO: 3; and

positions 76 ,155, 245, 270, 276, 348, 357, 430, 433, 460, 490 and 496 in the $P2X_7$ polypeptide as defined by the position in SEQ ID NO: 4;

and determining the status of the human by reference to polymorphism in $P2X_7$; and

ii) administering an effective amount of the drug.

9 An allelic variant of human $P2X_7$ polypeptide comprising at least one of the following:

a alanine at position 76 of SEQ ID NO 4;

a tyrosine at position 155 of SEQ ID NO 4;

a glycine at position 245 of SEQ ID NO 4;

a histidine at position 270 of SEQ ID NO 4;

a histidine at position 276 of SEQ ID NO 4;

a threonine at position 348 of SEQ ID NO 4;

a serine at position 357 of SEQ ID NO 4;

a arginine at position 430 of SEQ ID NO 4;

a valine at position 433 of SEQ ID NO 4;

a arginine at position 460 of SEQ ID NO 4;

a glycine at position 490 of SEQ ID NO 4; and

a glutamic acid at position 496 of SEQ ID NO 4;

or a fragment thereof comprising at least 10 amino acids provided that the fragment comprises at least one allelic variant.

10 An antibody specific for an allelic variant of human $P2X_7$ polypeptide as defined in claim 9.

11. A polynucleotide comprising any one of the following twenty six $P2X_7$ haplotypes:

	1012	489	5579	835	853	1068	1096	1405	1513
	SEQ ID 1	SEQ ID 2	SEQ ID 3	SEQ ID 2	SEQ ID 2	SEQ ID 2	SEQ ID 2	SEQ ID 2	SEQ ID 2
1	T	T	C	G	G	A	G	A	A
2	C	C	G	G	G	G	C	A	A
3	C	C	C	A	G	G	C	A	C
4	C	T	G	G	G	A	C	G	A
5	C	C	G	G	G	A	G	A	A
6	C	C	C	A	G	G	C	A	A
7	T	T	G	G	G	A	C	G	A
8	C	T	C	G	G	G	C	A	A
9	C	C	C	G	G	A	C	A	A
10	C	T	G	G	G	G	C	A	C
11	T	C	G	G	G	A	C	A	A
12	C	T	C	G	G	G	C	A	C

13	T	C	C	G	G	A	C	A	A
14	T	C	C	G	G	G	C	A	C
15	C	T	C	G	G	A	C	A	A
16	T	T	C	G	G	A	C	G	A
17	C	C	G	G	G	A	C	G	A
18	T	C	G	A	A	G	C	A	A
19	C	C	C	G	G	G	G	A	A
20	T	C	C	G	G	G	G	A	A
21	C	T	C	A	G	G	C	A	A
22	C	C	C	G	G	G	C	A	C
23	C	T	G	G	A	A	G	G	A
24	T	T	G	G	G	A	G	G	A
25	C	T	C	G	G	G	G	A	A
26	C	C	C	G	G	G	C	A	A

12 A human $P2X_7$ polypeptide comprising one of the following eighteen combinations of alleleic variant determined amino acids based on positions identified in SEQ ID NO: 4:

	155	270	276	348	357	460	496
1	Y	R	R	T	S	Q	E
2	Y	R	R	T	T	R	E
3	Y	R	R	T	T	Q	E
4	Y	R	R	T	S	R	E
5	Y	R	R	A	T	Q	A
6	Y	R	R	A	T	Q	E
7	Y	R	R	A	S	Q	E
8	Y	R	H	T	S	R	E
9	Y	H	R	A	T	Q	E
10	H	R	R	T	T	Q	E
11	H	R	R	T	T	R	E
12	H	R	R	A	T	Q	A
13	H	R	R	A	S	Q	E
14	H	R	R	A	T	Q	E
15	H	R	R	T	S	Q	E
16	H	H	R	A	T	Q	A
17	H	H	R	A	T	Q	E
18	H	H	H	A	T	Q	E

13 A polynucleotide which encodes any human $P2X_7$ polypeptide as defined in claim 12.

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